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ATTORNEY DOCKET NO. FIRST NAMED INVENTOR APPLICATION NO. FILING DATE PCS10361ADAM L 10/06/00 **HARLAND** 09/684,725 **EXAMINER** HM12/1102 GREGG C BENSON PAPER NUMBER **ART UNIT** PFIZER INC PATENT DEPARTMENT MS 1646 4159 EASTERN POINT ROAD **DATE MAILED:** GROTON CT 06340 11/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks** 

·								
	Application No.	Applicant(s)						
	09/684,725	HARLAND, LEE	HARLAND, LEE					
Offic Acti n Summary	Examiner	Art Unit	Art Unit					
	Ruixiang Li	1646	1646					
The MAILING DATE of this communication app Period for Reply	pears on the cover	sheet with the c rrespondence a	ddress					
A SHORTENED STATUTORY PERIOD FOR REPL THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1.1 after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a repl - If NO period for reply is specified above, the maximum statutory period - Failure to reply within the set or extended period for reply will, by statute - Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).  Status	136(a). In no event, howe by within the statutory mini will apply and will expire S e, cause the application to	ver, may a reply be timely filed  mum of thirty (30) days will be considered tim IX (6) MONTHS from the mailing date of this become ABANDONED (35 U.S.C. § 133).	ely. communication.					
1) Responsive to communication(s) filed on	·							
,	— nis action is non-fir	al.						
3) Since this application is in condition for allows closed in accordance with the practice under			the merits is					
Disposition of Claims								
4)⊠ Claim(s) <u>1-12 and 22</u> is/are pending in the ap	plication.							
4a) Of the above claim(s) 13-21 is/are withdraw	wn from considera	ion.						
5) Claim(s) is/are allowed.								
6)⊠ Claim(s) <u>1-12 and 22</u> is/are rejected.								
7) Claim(s) is/are objected to.								
8) Claim(s) 1-22 are subject to restriction and/or	election requireme	ent.						
Application Papers								
9)⊠ The specification is objected to by the Examine	er.							
10) $\boxtimes$ The drawing(s) filed on <u>10/06/2000</u> is/are: a) $\boxtimes$	accepted or b)☐ o	bjected to by the Examiner.						
Applicant may not request that any objection to the								
11)☐ The proposed drawing correction filed on	_ is: a)∏ approve	d b)  disapproved by the Exami	ner.					
If approved, corrected drawings are required in re		on.						
12) The oath or declaration is objected to by the Ex	caminer.							
Pri rity under 35 U.S.C. §§ 119 and 120								
13) Acknowledgment is made of a claim for foreign	n priority under 35	U.S.C. § 119(a)-(d) or (f).						
a) All b) Some * c) None of:	•							
1. Certified copies of the priority document								
2. Certified copies of the priority document								
<ul> <li>3. Copies of the certified copies of the prio application from the International Bu</li> <li>* See the attached detailed Office action for a list</li> </ul>	ireau (PCT Rule 1	7.2(a)).	ıl Stage					
14) Acknowledgment is made of a claim for domest	ic priority under 35	U.S.C. § 119(e) (to a provision	al application).					
a) The translation of the foreign language pro	• •							
Attachment(s)	, .,							
1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s)	5)	Interview Summary (PTO-413) Paper N Notice of Informal Patent Application (F Other:						

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#### **DETAILED ACTION**

#### Election/Restrictions

- 1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 1-12, and 22, drawn to polynucleotides, primers, vectors, host cells, and the process of making the polypeptide, classified in class 536, subclasses 23.1 and 24.33; class 435, subclasses 320.1, 325, and 69.1.
  - II. Claim 13, drawn to polypeptides, classified in class 530, subclass 324.
  - III. Claims 14 and 16, drawn to antibodies, classified in class 530, subclass 387.9.
  - IV. Claims 15 and 17, drawn to polypeptide modulators, classified in class 530, subclass 300.
  - V. Claim 18, drawn to a method of identifying peptide-binding compounds, classified in class 435, subclass 7.1.
  - VI. Claim 19, drawn to a method of treatment with antibodies, classified in class 424, subclass 134.1.
  - VII. Claims 20 and 21, drawn to a method of treatment with peptide modulators, classified in class 514, subclass 2.
- 2. The inventions are distinct, each from the other for the following reasons. Inventions I, II, III, and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01).
  In the instance case, the different inventions are drawn to completely different

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products having completely different structures and biological functions which are not interchangeable and which require non-cohesive searches and considerations.

- 3. Inventions V, VI and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). In the instance case the different inventions are drawn to completely different methods each having completely different method steps, using different compositions, and having completely different outcomes. The method of identifying peptide-binding compounds will not provide information regarding the method of treatment with either an antibody or a peptide modulator; On the other hand, the method of treatment with either an antibody or a peptide modulator will not be able to identify the peptide-binding compounds and the three methods are exclusive.
- 4. Inventions II and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the polypeptide may be used in materially different methods, such as production of antibody by immunization of the mice.
- 5. Inventions III and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially

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different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the antibodies may be used to detect or isolate the peptide.

- 6. Inventions IV and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptide modulators can be used in a binding assay or to study the biological functions of the peptide.
- 7. Invention I is an independent invention from V, VI, and VII; Invention II is an independent invention from VI and VII; Invention III is an independent invention from V and VII; Invention IV is an independent invention from V and VI. The different inventions are drawn to distinct product and method inventions.
- 8. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.
- 9. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

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10. Because these inventions are distinct for the reasons given above and the search

required for a single group is not required for any other group, restriction for

examination purposes as indicated is proper.

11. During a telephone conversation with Deborah A. Martin on August 9, a provisional

election was made without traverse to prosecute the invention of group I, claims 1-12

and 22. Affirmation of this election must be made by applicant in replying to this

Office action. Claims 13-21 are withdrawn from further consideration by the

examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected

invention, the inventorship must be amended in compliance with 37 CFR 1.48 (b) if

one or more of the currently named inventors is no longer an inventor of at least one

claim remaining in the application. Any amendment of inventorship must be

accompanied by a petition under 37 CFR 1.48 (b) and by the fee required under 37

CFR 1.17 (I).

Minor Objection to the Application

12. The title of the invention is not descriptive. A new title is required that is clearly

indicative of the invention to which the claims are directed. The following title is

suggested: "A Subtype of Neuromedin U Receptor".

Claim Rejections—35 USC § 101

13. 35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 1-12 and 22 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-12 and 22 are drawn to polynucleotides encoding G-protein-coupled receptors and methods of expressing these proteins. The claimed polynucleotides are not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not requires further research. The asserted utility of use of compounds (agonists or antagonists of the claimed polypeptide) in the manufacture of a medicament for treatment of obesity (page 8, line 36-page 8, line 11), while specific, is not substantial because it would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Likewise, the following asserted utility (page 9, lines 15-22) is not specific and substantial, "Drugs that modulate the novel PFI-002 receptor will therefore be likely to modulate signal transduction processes. It is therefore likely that modulators of the PFI-002 receptor may be useful for the treatment of many different disorders associated with signal transduction that will most likely include,

but not limited to, obesity, diabetes...". The word "likely" and the disclosure of a list of disorders in the specification clearly indicate that the asserted utility requires further research to determine the specific role of the claimed novel PFI-002 receptor in signal transduction processes and its association with a specific disorder.

In addition, the asserted utility of the PFI-002 polypeptide and nucleotide sequences encoding the polypeptide for screening drug candidates for treatment of diseases (page 9, lines 24-35) is not specific and substantial, either. Furthermore, the specification asserts that nucleotide sequences encoding a PFI-002 receptor provide probes to detect chromosomal aberration (page 19, lines 15-21). Since a disease specifically associated with an abnormal level of nucleotide sequences encoding a PFI-002 receptor has not been identified, the use of the probe to diagnose such chromosomal aberration would require further research. Thus, the asserted utility is not specific and substantial.

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Neither the specification as filed nor any art of record before the priority date of this application discloses or suggests any property or activity for the PFI-002 polypeptide and/or nucleotide sequences encoding the polypeptide such that another non-asserted utility would be well-established for the compounds.

15. Claims 1-12 and 22 are also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific and

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substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, even if the polynucleotide of SEQ ID NO: 1 or encoding a polypeptide of SEQ ID NO: 2 were to have a patentable use, the instant disclosure would not be found to be enabling for the claimed genus of homologues or fragments of the polynucleotides.

The factors to be considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. Ex Parte Forman, 230 USPQ 546 (Bd Pat. App. & Int. 1986); In re Wands, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Each of the claims recites a genus of polynucleotides that has at least 70% (75%, 80%, 85%, 90%, or 95%) identity to a polynucleotide comprising SEQ ID NO: 1 or encoding a polypeptide of SEQ ID NO: 2, as well as polynucleotides comprising fragments of a polynucleotide of SEQ ID NO: 1 or encoding SEQ ID NO: 2. However, other than SEQ ID NOS: 1 and 2, the disclosure does not provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown what modifications (e.g., substitutions,

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deletions or additions) one can make to SEQ ID NO: 1 or SEQ ID NO: 2 will result in mutants with the same function as SEQ ID NO: 1 or SEQ ID NO: 2. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the sequence of a peptide and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions and deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein.

The instant claims also embrace polynucleotide fragments of any size. However, the disclosure has not shown which portions or fragments of SEQ ID NO: 1 or SEQ ID NO: 2 are critical to the activity of the polypeptide encoded by the claimed polynucleotides. Thus, the disclosure has not provided sufficient guidance and information to enable one skilled in the art to predict which if any fragments of the whole molecule would be reasonably expected to retain characteristic activities alone. The general disclosure that one could make and use SEQ ID NO: 1 or SEQ ID NO: 2 could not be used to be such guidance as to guide one of skill in the art to make and use the invention commensurate in scope with the claims.

Accordingly, the disclosure fails to enable such a myriad of the claimed polynucleotides that not only vary substantially in length but also in amino acid composition and to provide any guidance to those skilled generally on how to make and use useful polynucleotides. Thus, it would require undue experimentation for one skilled in the art to make and use the polynucleotides embraced by the instant

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claims.

In addition, the disclosure provides the asserted use of four probes represented by SEQ ID NOS 3-6 in isolation of PFI-002 and determination of tissue distribution of PFI-002. However, since Claim 8, as it is written, comprises at least 15 contiguous nucleotides, it encompasses virtually any random sequence of any length as long as it has a stretch of at least 15 consecutive nucleotides that is the same as in the sequence(s) recited in claim 1. The state of the art is such that determining the specificity of hybridization probes is empirical by nature and the effect of mismatches within an oligonucleotide probe or primer is unpredictable. In view of the factors, the empirical and unpredictable nature of the art and the lack of guidance with respect to how to use other probes within the scope of the claim, the disclosure does not teach one skilled in the art how to successfully use probes of the claimed scope without undue experimentation.

## Claim Rejections—35 USC § 112, 1st paragraph

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-12 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

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The description discloses a nucleotide sequence set forth in SEQ ID NO: 1, which encodes a polypeptide as set in SEQ ID NO: 2. However, each of these claims as written includes a genus of polynucleotides that has at least 70% (75%, 80%, 85%, 90%, or 95%) identity to a polynucleotide comprising SEQ ID NO 1 or encoding SEQ ID NO 2, or a polynucleotide encoding the polypeptide expressed by the DNA contained in the clone deposited as NCIMB 41066. Thus, the claims encompass a huge number of polynucleotides that vary substantially both in length and in amino acid composition.

The instant disclosure of a single species of nucleic acid of SEQ ID NO: 1 encoding a single polypeptide of SEQ ID NO: 2 does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art

does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed polynucleotides as being identical to those instantly claimed.

Due to the breadth of the claim genus and lack of the definitive structural or functional features of the claimed genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus.

## Claim Rejections—35 USC § 112, 2<sup>nd</sup> paragraph

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 1, 8, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it recites an abbreviated term, "NCIMB", which should be spelled out in the claim. In addition, the claim can be more clearly stated as "a polynucleotide encoding the polypeptide expressed by the DNA contained in the clone deposited as National Collections of Industrial and Marine Bacteria Limited (NCIMB) 41066";

Claim 8 is vague and indefinite because it is not clear which polynucleotide of claim 1 is referred to by "said polynucleotide".

Claim 22 is indefinite because it uses the words" and/or" to describe an animal cell genetically modified to increase or decrease the expression of a polynucleotide sequence.

20. Claim 22 is also objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 22 depends on an unelected claim (Claim 13). For prosecution purpose, the examiner considers as if it depends upon Claim 1.

### Claim Rejections—35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- 22. Claims 1-10 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Database EMBL Accession No. AC008571 (August 3, 1999), which discloses a nucleotide sequence comprising SEQ ID NO: 1 (See attached sequence alignment) as well as a nucleotide sequence capable of hybridizing to the nucleotide sequence. The nucleotide sequence is present in a vector which in turn is present in a host cell, meeting the limitation of claims 9, 10, and 22.

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- 23. Claim 1 is also rejected under 35 U.S.C. 102(b) as being anticipated by Lubert Stryer (*Biochemistry*, 3<sup>rd</sup> Edition, pp71-90, W. H. Freeman, 1988). Stryer teaches the structure of nucleotides, DNA, and RNA. Claim 1 recites "a polynucleotide fragment" which encompasses just about everything, from a single nucleotide to at least SEQ ID NO: 1 or its complement. Thus, the reference by Stryer anticipates Claim 1.
- 24. Claims 1, 7-12, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Tan, et al (IDS, paper #7). Tan et al disclose a nucleotide sequence of a human G-protein-coupled receptor (FM3) with two regions that contain 19 and 26 contiguous nucleotides identical to that set forth in SEQ ID NO: 1 (See attached sequence alignment). Also disclosed are a nucleotide sequence of mouse G-protein-coupled receptor (FM3) with 15 contiguous nucleotides identical to that set forth in SEQ ID NO: 1 (See attached sequence alignment) and the use of a radiolabled probe encompassing mouse FM-3 ORF in determining the expression profile of FM3 mRNA in several mouse tissues (See Fig. 3, page 228). Furthermore, Tan, et al disclose transfected HEK-293 cells expressing FM3 (cell membrane expression of FM3; See page 228, column 1, lines 24-27), which meets the limitation of claims 10-12 and 22.
- 25. Claim 12 is also rejected under 35 U.S.C. 102(b) as being anticipated by Maniatis et al (*Molecular Cloning: A laboratory Manual*. 2<sup>nd</sup> Edition, Book 3, pp17.37-17.41, Cold Spring Harbor Laboratory Press, 1989). Maniatis et al. teach membrane preparation of a cell by centrifugation and thus the reference meets the limitation of

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claim 12, which encompasses membrane preparations indistinguishable from those of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li Examiner October 16, 2001

> YVONNE EYLER, PH.D SUPERVISORY PATENT EXAMINER TECHNOLOGY CENTER 1600

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COMMENT

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Web site:

http://www.jgi.doe.gov

Project Information Center Project Name: 396672, H361 Center clone name: CIT-HSPC\_550M4

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Direct Submission
Submitted (03-AUG-1999) Production Sequencing Facility, DOE Joint Submitted (13-AUG-1999) Production Sequencing Facility, DOE Joint Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA On May 5, 2000 this sequence version replaced gi:7211884.
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1 (bases 1 to 216673)

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Consensus quality: 210803 bases at least Q20
Estimated insert size: 223000; pulse field gel estimation
Estimated insert size: 215873; sum-of-contigs estimation
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Quality coverage: 5.64 in Q20 bases; pulse field gel estimation
Quality coverage: 5.64 in Q20 bases; pulse field gel estimation.
* NOTE: This is a 'working draft' sequence. It currently
* consists of 9 contigs. The true order of the pieces
* is not known and their order in this sequence record is
* arbitrary, Gaps between the contigs are represented as
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128195 Sequence 1
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128196 Sequence 19
112398 Homo sapien
120932 Sequence 5
128197 Sequence 2
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AB017027 Mus muscu
X51657 B. taurus do
AF149717 Rattus no

SSU60180 SSU60178 I15508 I89330 I20930 I28195

BTD2DOR AF149717 AB015645

ALIGNMENTS

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/ Yelle " NMUZK" / note "FM-4" / codon_start=1 / codon_start=1 / product = "neuromedin U receptor 2" / protein_id = "AAF82755.1" / db_xref="G1:0982156" / translation = "MEKLONASWIYOQKLEDPFOKHLNSTEEYLAFLCGPRRSHEFLP VSYVYVPIFYNGYIGNYLVCLYILOHQAMKTPTNYYLFSLAVSDLLVLLLGMPLEVYE WEBNYDEI FCONCCYTENT TOTALOHQAMKTPTNYYLFSLAVSDLLVLLLGMPLEVYE	,	•
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/db_xref="taxon:9606" /chromosome="5" 1. 1239	gene	
Location/Qualifiers e 1. 1239 /organism="Homo sap	sourc	72
Submitted (09-mar-2000) Pharmacology, Merck Research Labs, West Point, PA 19486, USA	i	
<pre>2 (bases 1 to 1239), Llu,Q., McDonald,T.P., Wang,R., Jlang,Q. and Howard,A.D. Direct Submission</pre>	AUTHORS TITLE	-
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to 1239)	REFERENCE	
Homo Sapiens	SOURCE ORGANISM	٠,٠
AF242874 1239 bp mRNA PRI 13-JUL-2000 N Homo sapiens neuromedin U receptor 2 (NMUZR) mRNA, complete cds. AF242874 GI:9082155	AF242874 LOCUS DEFINITION ACCESSION VERSION KEYWORDS	
AGTATCTAG 83675	83683 SULT 2	
TCTACCTCC	83743	
tgtacggtcatcaagcccatgtggatctacaatttcatcatccaggtcacctccttcct	03 01	_
atccatggcatcaagttccactacttccccaatgggtccctggtcccaggttcggccacc 600 	Qy 541 Db 83863	
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	Qy 421 Db 83983	
	Db 84043	

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FROMIG of: /home/bobryen/big/US09684725.seq sequence 1, application us/09684725 general information: applicant: lee harland title of invention: novel polypeptide file reference: pcs1036ladam . . .
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Identification and Functional Characterization of a Novel Subtype
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                                                                                                                                                                                                                                 Submitted (16-JAN-1998) Biochemistry and Physiology, Inc., P.O. Box 2000, Rahway, NJ 07065, USA
                                                                                                                                                                                                                                                             Direct Submission
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1 (bases 1 to 1318)

Raddatz,R., Wilson,A.E., Artymyshyn,R., Bonini,J.A., Borowsky,B. Botely,L.W., Zhou,S., Kouranova,E.V., Nagorny,R., Guevarra,M.S., Dai,M., Lerman,G.S., Vaysse,P.J., Branchek,T.A., Gerald,C., Forray,C. and Adham,N.
                                                                                                           Submitted (25-MAY-2000) Target | Pharmaceutical Corporation, 215
                                                                                                                                                                                                          Nervous System
J. Biol. Chem.
                                                                                                                                                                                                                                     Identification and Characterization of Two Neuromedin U Receptors Differentially Expressed in Peripheral Tissues and the Central
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Avsdllvllvglplelyemmhnypfilgvggcyfrtilfemvclasvlnvtalsvery
VAVVHPJQARSWYTRAHVRRVLGA-WNGLAMLCSLPNTSLHGIRQLHVPCRGPVPDSAV
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-308 -228 -148

TT CA	TGC	ACTO CTCT	CGAA	TACT	CTGT	AGTI CTT	rgaa? Agga	ATGCA CAGAC	CTG	PAGTO	GCGCA GGTC GCTCT	GCAC	ATGC GACT	TTTCTC	TTTC GGT#	CCAC	TGGC	ATGI	GACI	'AAT	-22 -14 -69 -1	19
	-	CTG L	GTC V	TGC C	aat N	ATC I	agt s	GAG E	TTC F	AAG K	TGG W	CCC P	TAT Y	CAA Q	CCT P	GAG E	GAT D	CTG L	AAC N	L	ACC T	60 20
	61 21		GAG E	GCC A	CTG L	AGG R	CTG L	AAG K	TAT Y	TTG L	GGG G	CCA P	CAG Q	CAG Q	ATG M	AAA K	CAG Q	TTT F	GTC V	P CCC	ATC I	120 40
	121 41		GTC V	ACG T	TAC Y	CTG L	CTG L	ATC I	TTC F	GTG V	GTG V	GGC G	ACT T	L	G	AAC N	GGG G	CTG L	ACC T	TGC C	ACC T	180 60
;	181 61		ATC I	CTG L	CGC R	AAC N	AAG K	ACT T	ATG M	CGC R	ACG T	CCC P	ACC T	TM AAC N	_	TAC Y	CTC L	TTC F	AGC S	CTC L	GCT A	240 80
;	241 81		TCC S	GAT D	ATG M	CTG L	GTG V	CTC L	CTG L	GTG V	GGC G	TTG L	CCT P	CTG L	GAG E	CTT L	TAT Y	GAG E	ATG M	CAG Q	CAA Q	300 100
	301 101		TAC Y	CCG P	TTC F	CAG Q	CTG L	GGT G	GCG A	AGT S	GCC A		1-3 — TAC Y	TTC F	CGA R	ATA I	CTG L	CTC L	TTA L	GAG E	ACC T	360 120
	361 121		TGC C	CTA L	GCT A	TCA S	GTG V	CTC L	AAT N	GTC V	ACA T	GCC A	CTG L	AGT S	GTG V	GAG E	CGT R	TAT Y	GTG V	GCC A	GTG V	420 140
	121		CGC	CCA P		CAA			тст	GTG V	ATG	ACA	CGG	GCC			CGC	TM CGC	4 ATG			480
			R		L GTC	Q	A GCT	ACT	S	•	тст	T CTG	CCC	AAC	ACC	V AGC	R	R - CAT	M GGC	Ť	g agt	160 540
	161		I	W ACT	Curc.	L	A	T	L	F	S GTG	L	P	N TCA	T	S	_	H	G	L	S	180
	181		L	T	V	P	C TM-	R	G	P	V	P	D	S	A	I	C	S	L	V	GGT	200
	501 201		ATG M	GAC D	TTC F	TAC Y	AAG K	TTG L	gtg V	GTA V	CTG L	ACT T	ACC T	GCA A	CTG L	CTC L	TTC F	TTC F	TGT C	CTG L	CCC P	660 220
	661 221		GTC V	ACC T	ATC I	AGT S	GTG V	CTG L	TAT Y	CTG L	CTC L	ATT I	GGG G	CTG L	CGG R	CTG L	CGG R	AGG R	gag E	agg R	ATG M	720 240
	721 241		CTC L	CAA Q	GTG V	GAG E	GTC V	AAG K	GGC G	AGG R	AAA K	ACC T	GCA A	GCA A	T	Q	GAG E	ACC T	TCC S	CAC H	AGA R	780 260
	781 261		ATT I	CAG Q	CTG L	CAA Q	GAT D	AGG R	GGA G	CGG R	AGA R	CAG Q	GTG V	ACC T	TM AAG K	•	CTG L	TTT F	GCA A	CTG L	GTT V	840 280
	841		GTA V	TTC F	GGC G	ATC I	TGC C		GCT A	CCA P	TTC F	CAT H	GCT A	GAC D	CGT R	ATC I	ATG M	TGG W	AGC S	CTG L	GTG V	900 300
	01			CAC H	TCA S	ACG T	GAA E		CTG L	CAC H	CTG L	GCC A	TAC Y	CAG Q	TGT C	GTC V		-7 ATT I	GCC A	TCT S	GGC G	960 320
	61			TTC F	TAT Y	CTC L	GGC G				AAC N				TAC Y			ATG M	TCT S		CGC R	1020 340
	21		CGA R		ACC T	TTC F	CTG L	CAA Q	GCC A	CTG L	GGC G	CTT L	GGA G	ACC T	CAG Q	TGC C	TGT C	CAT H	CGC R	CGC R	CAA Q	1080 360
			TAT	CAT	GGC G				CAC H		AGG R	TTG L	ACC T	ACA T	GGC G	AGC S	ACC T	CTG L	TGT C		GTG V	1140 380
		GGC G									CTG L				GAG E						CAA Q	1200 400

**FIG. 1.** DNA and deduced amino acid sequence for mouse (A) and human (B) FM-3. Putative transmembrane  $\alpha$  helices are overlined and numbered from 1 to 7. For the murine form, a noncanonical leucine codon is postulated to serve as the initiator.

1218

406

1201 GAG ACA GAC CCC TCC TGA

D P

s \*

401 E T

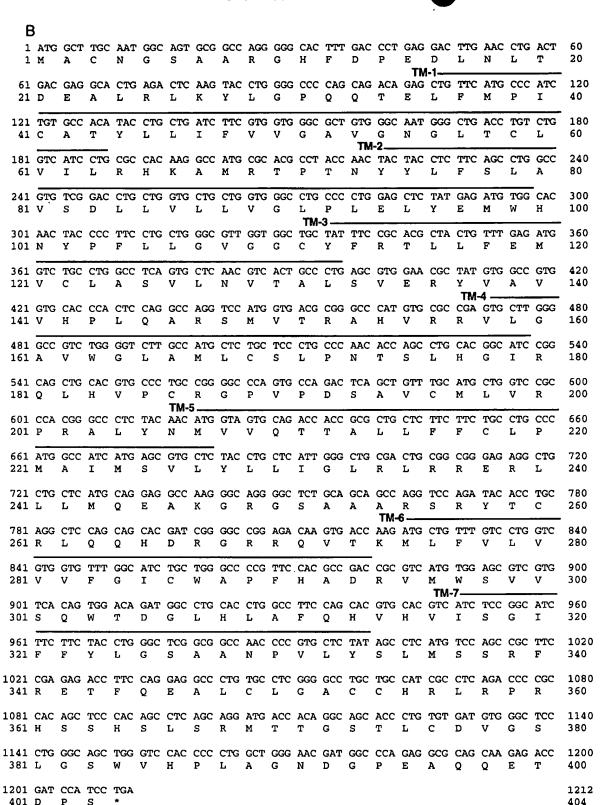


FIG. 1—Continued

GenBank databases were monitored daily using the Tblastn program (1) with amino acid sequence from the human GHS-R TM domains 6–7 (residues 265–366). A mouse EST (dEST database Accession No. AA562357, deposited August 18, 1997) derived from a T-cell library was identified with a significant homology score. EST 562357 exhibited good sequence identity (63%)

DNA, 36% amino acid) to the 3' end of the gene for the human GHS-R. A murine T cell  $\lambda$ XR cDNA library (Stratagene) was screened with the mouse EST 562357 probe (455 bp in length) under high-stringency conditions. Four partial clones were identified after three rounds of screening. Additional clones were isolated from mouse thymus poly(A)<sup>+</sup> RNA via 5' Race Mara-